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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 09/327,761
Filing Date: June 07, 1999
Appellant(s): PETERSEN ET AL.

Christopher M. Humphrey
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed July 11, 2005 appealing from the Office
action mailed December 15, 2004.

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(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner that may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

Two of the references cited by the examiner are also relied upon in Examiner's Answers addressing the rejection of the pending claims of U.S. Appl. No. 09/947,833, filed September 6, 2001, and U.S. Appl. No. 10/060,697, filed January 30, 2002.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is substantially correct. The changes are as follows: The examiner's answer contains new grounds of rejection set forth in Section (9) below.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

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(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection***Prior Art of Record***

6,030,635	Gertzman et al.	2-2000
3,858,887	Yim et al.	1-1995
5,484,601	O'Leary et al.	1-1996
GB999,487*	Baillie et al.	7-1965

*cited for rebuttal purposes only and not as part of the prior art rejection of record

The following ground(s) of rejection are applicable to the appealed claims:

Claims 2-3, 12-21 and 35-38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of O'Leary et al. (5,484,601), Yim et al. (5,385,887) and Gertzman et al. (6,030,635) taken as a whole for the reasons of record.

The claims are drawn to **bone graft substitute composition** that comprise

- broadly **calcium sulfate**, and specifically calcium sulfate hemihydrate,
- broadly **a mixing solution**, and specifically those defined in claims 13-15,
- broadly **a cellulose derivative**, and specifically those defined in claim 16, and
- **demineralized bone**.

Dependent claims also recite ranges of amounts of each ingredient as well as including as a further ingredient, bone allograft. Claim 35 recites a method of making a bone graft substitute which requires that a calcium sulfate, cellulose derivative and

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demineralized bone composition is mixed with the mixing solution to form a bone graft substitute. Dependent claims further include bone allograft as an additional ingredient, require the consistency of the bone graft substitute made by the claimed method to be in the form of a putty and further defining the specific forms of the ingredients.

O'Leary et al. disclose a flowable demineralized bone matrix composition for use in bone repair. O'Leary et al. state at col. 1, lines 36-43 that

"[I]t is a particular object of the invention to provide a composition of liquid or pastelike consistency comprising demineralized osteogenic bone powder and a biocompatible liquid synthetic organic material as a carrier for the bone powder with or without such optional ingredients as thixotropic agents, medicaments, and the like, and to apply the composition at a bone defect site to induce new bone ingrowth at the site."

At col. 3, lines 14-20, the patent states

"[t]o provide the demineralized allogeneic bone powder composition of this invention, the demineralized bone powder with or without any of the foregoing optional components mentioned above absorbed therein is combined with a biocompatible liquid synthetic organic material which functions as a carrier or suspension agent for the bone powder."

The patent further defines the terms "liquid" and "flowable" as

"intended to include (1) organic materials which in the pure or highly concentrated state and at ambient temperature, e.g., 15-40° C. are flowable liquids and (2) organic materials which in the pure or concentrated state and at ambient temperature are normally solid but dissolved in a suitable solvent, e.g., water or a biocompatible organic solvent such as ethanol, can be provided in liquid form. Functionally, the liquid component of the composition serves to provide a flowable material of widely varying consistency. The term "flowable" as used herein applies to compositions whose consistencies range from those which can be described as shape-sustaining but readily deformable, e.g., those which behave like putty, to those which are runny. Specific forms of flowable bone powder compositions include cakes, pastes, creams and fillers."

O'Leary et al. disclose at col. 3, line 56 to col. 4, line 6 that

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“[w]here, in a particular bone powder composition, the bone powder has a tendency to quickly or prematurely separate from the carrier or to otherwise settle out from the composition such that application of a fairly homogeneous composition is rendered difficult or inconvenient, it can be advantageous to include within the composition a substance whose thixotropic characteristics prevent or reduce this tendency. Thus, e.g., where the carrier component is glycerol and separation of bone powder occurs to an excessive extent where a particular application is concerned, a thickener such as a solution of polyvinyl alcohol, polyvinylpyrrolidone, cellulosic ester such as hydroxypropyl methylcellulose, carboxy methylcellulose, pectin, food-grade texturizing agent, gelatin, dextran, collagen, starch, hydrolyzed polyacrylonitrile, hydrolyzed polyacrylamide, polyelectrolyte such as polyacrylic acid salt, etc., can be combined with the carrier in an amount sufficient to significantly improve the suspension-keeping characteristics of the composition.”

The patent also discloses further limitations of the claims. For example, the claims require the presence of 10-100 parts by weight of demineralized bone matrix. O’Leary et al. teach at col. 4, lines 18-22 that

“[t]he amount of bone powder which can be incorporated into the composition of this invention can vary widely with amounts of from about 5 to about 80 weight percent, and preferably from about 20 to about 60 weight percent, being entirely suitable in most cases.”

That which the specification defines as a “plasticizing substance” (cellulosic esters such as hydroxypropyl methylcellulose and carboxy methylcellulose) is identified as included in the composition of O’Leary as a thixotropic agent.

Finally, O’Leary et al. disclose at col. 2, line 53 to col. 3, line 13, that

“[a]ny of a variety of substances can be introduced into the [demineralized] bone particles” and includes a non-limiting list which includes inorganic elements, parenchymal cells, growth factors, bone morphogenic proteins, and mesenchymal elements. O’Leary’s composition may include other suitable ingredients such as bone morphogenic proteins, growth factors, therapeutic agents, and cells.

Therefore, O'Leary et al. provides the disclosure to produce a **bone graft substitute composition** containing a **mixing solution**, a thixotropic agent (claimed as plasticizing substance) which is defined by the patent as a **cellulose derivative** and **demineralized bone**. O'Leary teaches that this bone graft substitute may be prepared in multiple forms from liquid to paste-like depending upon the requirements of the practitioner. O'Leary does not, however, explicitly state that calcium sulfate is included in the bone graft substitute composition.

Yim et al. discloses **bone graft substitute compositions** that are formulated for delivery of osteogenic proteins. These formulations contain **calcium sulfate hemihydrate** combined with **cellulose materials** (claimed as cellulose derivatives).

Yim et al. further teach that the addition of a calcium sulfate hemihydrate-containing substance (CSHS) reduces setup time and provides improved moldability and consistency to a bone graft substitute formulation.

Yim et al. state that the osteogenic proteins can be utilized in the form of a pharmaceutically acceptable solution and cites sodium chloride as an appropriate solubilizing agent, as well as multiple different aqueous solutions of amino acids and other acids. See col. 3, line 53. Further, at col. 4, lines 32-33, the osteogenic protein formulations may be lyophilized and reconstituted with water prior to use. Yim et al. also include a "porous particulate polymer matrix component" that acts as an "in situ scaffolding for the osteogenic protein, while having biodegradable properties allowing for replacement by new bone growth" as well as a "protein-sequestering material". This material is used to "hold" the osteogenic proteins at the site for a sufficient time to

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allow them to have a bone growth promoting effect. Suitable "protein-sequestering agents" are disclosed at col. 7, lines 25-34, as cellulosic materials such as alkylcelluloses (including hydroxyalkylcelluloses), such as methylcellulose, ethylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, and carboxymethylcellulose." The cellulosic protein sequestering agent is preferably present in a concentration of about 2 to about 10% (w/v).

Determination of the quantity of the calcium sulfate hemihydrate is disclosed as being well within the skill of the practitioner and is determined to be that quantity which provides the best handling properties both immediately after and 1 to 2 hours after preparation will be optimal. The formulations of the disclosure of Yim et al. provide

"malleable implants that allow therapeutically effective amounts of osteoinductive protein to be delivered to an injury site where cartilage and/or bone formation is desired. Such an implant may be used as a substitute for autologous bone graft in fresh and non-union fractures, spinal fusions, and bone defect repair in the orthopaedic field; in cranio/maxillofacial reconstructions; for prosthesis integration, especially as a surface coating to improve fixation of prosthetic implants such as hydroxylapatite coated prostheses; in osteomyelitis for bone regeneration; and in the dental field for augmentation of the alveolar ridge and periodontal defects and tooth extraction sockets. When used to treat osteomyelitis or for bone repair with minimal infection, the osteogenic protein may be used in combination with porous microparticles and antibiotics, with the addition of protein sequestering agents such as alginate, cellulose, especially carboxymethylcellulose, diluted using aqueous glycerol."

Therefore, Yim et al. provides the disclosure of a **bone graft substitute composition**, similar to O'Leary et al., which contains **calcium sulfate hemihydrate**, a mixing solution, and a protein sequestering substance which can be a **cellulose derivative** and which has improved moldability and consistency. While Yim et al. does not explicitly disclose the use of demineralized bone matrix, the bone morphogenic

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proteins of the Yim reference, while not identical in composition to demineralized bone of the claims, serves the same purpose, i.e. the delivery of bone growth promoting proteins to a site of bone injury. Bone morphogenic proteins are present in demineralized bone matrix, and are obtained via extraction of demineralized bone matrix. The patent also discloses further limitations of the claims. For example, the claims require specific mixing solutions. Yim et al. discloses, in a non-limiting list, both water and sodium chloride as a solvent present in the composition for the osteogenic proteins. Since calcium sulfate hemihydrate (plaster of paris) requires an aqueous solution to activate it and allow it to harden, one of ordinary skill in the art would be aware such a solution would be necessary and the selection of either sterile water or saline or other buffers is deemed conventional and well within the skill of the practitioner. To that end, it is noted that the patent to Yim et al. clearly acknowledges that a composition containing calcium sulfate hemihydrate must be kept dry until the time of its use since the addition of an aqueous solution causes the activation of the calcium sulfate hemihydrate and results in ultimate hardening of the calcium sulfate hemihydrate (such as seen with the use of plaster of paris). Yim et al. state at col. 8 that

“[t]he osteogenic protein and porous particles of the formulations may be provided to the clinic as a single vial formulation, either as a solution or in lyophilized form, or the formulation may be provided as a multicomponent kit wherein, e.g. the osteogenic protein is provided in one vial and the porous particles and calcium sulfate hemihydrate-containing substance each are provided in separate vials.”

Further, Yim et al. discloses the mixing of the osteogenic proteins in solution with the calcium sulfate hemihydrate. The aqueous solvent of the osteogenic proteins, such as

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water or sodium chloride, would be expected to activate the calcium sulfate hemihydrate.

The claims also require the presence of approximately 1 to 40 parts of the plasticizing substance by weight. Yim et al. teaches at col. 7, lines 40-45, that the cellulosic protein sequestering agent is preferably present in 2-10% (w/v). The claims define the specific cellulose derivatives. Plasticizing substances such as recited in the claims are identified as included in the composition of Yim et al. as a protein sequestering agent.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of O'Leary et al. with components of the composition of Yim et al. Both O'Leary et al. and Yim et al. have the same object in creating a malleable, workable bone growth promoting composition. One of ordinary skill in the art when reviewing the disclosure of Yim would have been motivated to include a calcium sulfate component into the composition of O'Leary et al. with the expected benefit disclosed by Yim et al., i.e. that a calcium sulfate component would add improved handling, moldability and consistency to the formulation of O'Leary as well as reducing the set up time. The compositions of Yim and O'Leary are so sufficiently similar that one of ordinary skill in the art at the time the invention was made would be aware of the properties of the calcium sulfate hemihydrate would not impair or otherwise negatively affect the components of the O'Leary composition, which is evidence that one of ordinary skill in the art would have had a reasonable expectation of success in the addition of the calcium sulfate hemihydrate to the

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composition of O'Leary. Both compositions contain components that provide either directly or indirectly osteogenic proteins, and both compositions contain a cellulosic material that is being used for the same purpose, i.e. to impart viscosity and suspension properties to the respective compositions. The general amounts of both the demineralized bone matrix and the cellulose material are taught by the references. The optimization of the amount of calcium sulfate and mixing solution to be further included is deemed well within the skill of the practitioner at the time the invention was made as it is clear that the amount of calcium sulfate is directly related to desired rate of set up of the composition, i.e. the more calcium sulfate used, the faster the composition will set up and harden. Further, since the amount of water that is needed to hydrate any given amount of calcium sulfate hemihydrate is known, it is well within the skill of the practitioner to infer that the amount of mixing solution present is inversely related to the desired set up time and directly proportional to the ultimate consistency of the composition, i.e. the less mixing solution used, the less dilute the calcium sulfate and the faster the set up time of the composition. As a result, the composition will be more paste-like in consistency. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) ("[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."). While it is noted that a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation, as evidenced above, the prior art

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recognizes the results produced by the claimed components and teaches ranges of the claimed ingredients that overlap the claimed ranges. See *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980).

While claims 2-3, 13-20, 35, and 37-38 do not require the presence of allograft bone and while it can be concluded that these claims could be properly rejected under the combination of the patents to O'Leary and Yim, alone, it is noted that the inclusion of Gertzman in the rejection of these claims does not effect the propriety of the rejection. Reliance on any given number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). Both O'Leary and Yim teach that other conventional components included in bone growth promoting compositions may be included in the disclosed compositions and the claims are couched in open transitional phrasing. Claims 21 and 36 require the further inclusion of bone allograft. The patent to Gertsmann et al. teaches another malleable paste **bone graft substitute composition** for filling bone defects. In the Background of the Invention, the reference teaches at col. 1 the various substances are known to be included in a bone growth promoting composition. Included in this list is autologous bone, bone marrow, blood, calcium sulfate, and **allograft bone**. It would have been obvious to one of ordinary skill in the art at the time the invention was made to further include allograft bone in the composition of O'Leary as modified by Yim. One of ordinary skill in the art would have been motivated to include the allograft bone in order to maximize the bone growth promoting activity of the composition for the expected benefit of the addition of the

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"building blocks" of new bone, i.e. collagen fiber reinforced hydroxyapatite matrix containing active bone morphogenic proteins at an area in need thereof. One of ordinary skill in the art would have had a reasonable expectation of success since the composition of Gertzman is structurally and functionally similar to both the composition of O'Leary and the composition of Yim.

New Grounds of Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2, 12, 15, 16, 18, and 35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4-7, 17-18, 20-22, and 25 of U.S. Patent No. 6,652,887.

Each of the elements of the patented claims is either the same as the elements of the instant claims or is a species of the generic elements of the instant claims.

While no composition claim recites a composition comprising both a cellulose derivative as the plasticizing substance and a mixing solution, it would have been

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obvious to select a cellulose derivative as the plasticizing substance of the referenced claims because the claims recite a cellulose derivative as an appropriate plasticizing substance choice; further, per the method claim 23, a mixing solution is required to activate the referenced bone graft substitute.

Claims 2-3 and 12-21 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 and 9-24 of copending Application No. 09/947,833. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-22 of the referenced application recite species of the instant generic claims drawn to the composition and therefore anticipate them.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 2-3, 8, 12-27, 29 and 32 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-30 of copending Application No. 10/060,697.

Each of the elements of the patented claims is either the same as the elements of the instant claims or is a species of the generic elements of the instant claims. It would have been obvious to select a cellulose derivative as the plasticizing substance of the referenced claims because the referenced claims recite a cellulose derivative as an appropriate plasticizing substance choice.

This is a provisional obviousness-type double patenting rejection.

(10) Response to Argument

Appellants argue that there is no motivation to combine the references; however, Appellants' arguments are made against each the reference individually. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Specifically, Appellants assert that there is no motivation to combine the calcium sulfate hemihydrate of Yim with the composition of O'Leary. Further, Appellants appear to be asserting that O'Leary teaches away from the combination by stating that

"there is nothing in O'Leary to indicate that a composition that hardens or sets over time is envisioned. In fact, the reference suggests otherwise by describing the term "flowable" as including compositions with consistencies ranging from those that are "shape sustaining but readily deformable . . . to those which are runny" (column 3, lines 30-34). Further, we note that O'Leary suggests the use of a thickener if settling of the bone powder within the organic liquid is a problem. (column 3, lines 56-63). This also suggests that the composition is intended to maintain a liquid, flowable state for an extended period of time. Obviously, if the composition is intended to set into a hardened mass within a short period of time, settling would not be an issue.

Appellants' arguments are drawn only to the O'Leary reference and fail to address the rejection made over the references as a whole. The theme of Appellants' arguments about the patent to O'Leary revolve around Appellants' use of the terms "extended period of time" and "short period of time" as a requirement of the composition of O'Leary; however, these terms do not appear in the patent. In absence of these terms in the patent to characterize the object of the invention of O'Leary and since all bone graft compositions of the prior art are desired to be maintained in place to stimulate replacement by mineralized (and therefore hardened) bone tissue, Appellants'

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arguments are simply not germane to the rejection of record. See particularly, col. 1, lines 40-43 where the object of the invention is "to apply the composition at a bone defect site to induce new bone ingrowth at the site." New bone growth is not immediate and requires time; for example, bone growth to repair fractures takes up to three months for complete bone replacement in the area of the fracture. As a result, one of ordinary skill in the art would interpret the term "flowable" as used by O'Leary to describe the condition of the composition for the purpose of handling of the composition during application to the bone defect. It would not reasonably be interpreted as a condition that is required to be maintained throughout the time period that the composition spends in situ at the bone defect.

Appellants further argue that

"we note that O'Leary suggests the use of a thickener if settling of the bone powder within the organic liquid is a problem. (column 3, lines 56-63). This also suggests that the composition is intended to maintain a liquid, flowable state for an extended period of time. Obviously, if the composition is intended to set into a hardened mass within a short period of time, settling would not be an issue."

There is no evidence of record to support these assertions. Appellants are first reminded that O'Leary is using bone powder of an average particle size from about 0.1 to 1.2 cm. Demineralized bone is composed of the osteoid components of bone that are composed of large, relatively insoluble proteins such as collagen. Bone particles of this composition and size cannot and will not dissolve in the disclosed carriers. Settling relates to the homogeneity of the bone powder distribution in a carrier. Therefore, only bone powder suspensions can be formed and O'Leary is explicit that homogeneity and settling are important issues. Appellants are further reminded that the rejection

maintained that one of ordinary skill in the art would be motivated to add the calcium sulfate hemihydrate to the composition of O'Leary. Hydrated calcium sulfate hemihydrate does not harden instantaneously and O'Leary states that the bone powder has a tendency to "quickly" separate from the carrier. Clearly, this "quick" separation occurs even during preparation and therefore before the application of the bone graft composition to the bone defect. Therefore, it can clearly be concluded from the disclosure of O'Leary that the thickener is required regardless of any other components.

Therefore, Appellants' arguments that the "teachings of O'Leary are manifestly inconsistent with the well-known properties of calcium sulfate hemihydrate solutions" and that "the addition of calcium sulfate hemihydrate to the O'Leary composition would have been avoided by one of skill in the art since the resulting composition would not have been expected to maintain a flowable state for an extended period of time, which is clearly the aim of the reference" are not supported by the disclosure of O'Leary and therefore not persuasive.

Appellants assert that "[a]lthough Appellants have discovered that the claimed plasticizing substance can forestall the calcium sulfate hemihydrate hardening reaction, this effect is not appreciated in the prior art of bone graft substitute compositions." This statement is not completely accurate; in two related applications (10/060697 and 09/915997), the examiner cited GB 999,487 as evidence that cellulose derivatives such as methyl sodium carboxymethyl cellulose are known as set retardants for calcium sulfate hemihydrate (plaster of paris). **Appellants are advised that this reference is not cited herein as being used in the rejection but merely to rebut a statement**

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made in Appellants' brief. Notwithstanding Appellants' inaccurate statement, there is, in actuality, no need to identify the set retardation effects of the "plasticizing substance" in any of the prior art references since the references, taken as a whole, provide the motivation to combine the calcium sulfate hemihydrate of Yim with the composition of O'Leary. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Wiseman*, 596 F.2d 1019, 201 USPQ 658 (CCPA 1979). See also *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985) ("The fact that appellant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.").

Appellants further assert that

As a result, one of ordinary skill in the art without the benefit of Appellants' disclosure would view the combination of calcium sulfate hemihydrate with the O'Leary formulation as likely to negate the flowability requirement set forth in O'Leary. Thus, for this reason, one of ordinary skill in the art would not find the requisite motivation to combine the calcium sulfate hemihydrate of Yim with the O'Leary composition.

Appellants appear to be suggesting that O'Leary must identify the problem in order to provide the motivation to solve it; however, there is no requirement in the patent law as to which specific piece of prior art provides the motivation to combine the references.

"There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). So long as at least one of the prior art references provides the motivation, the requirements of the statute are met.

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Further, Appellants also err in requiring that any prior art document must explicitly identify a problem to be solved in another specific formulation in order to provide motivation. Yim shows that bone repair compositions that do not contain CSHS will have improved moldability upon the inclusion of the CSHS and provides a reasonable expectation of success based upon the known properties of CSHS. This teaching is not negated simply because Yim does not identify all specific extant bone repair formulations that do not contain CSHS. Again, such a requirement is not consistent with existing patent law and would, in fact, be onerous.

Appellants further state that

Even ignoring the clear suggestion in the art to avoid combining calcium sulfate hemihydrate with O'Leary as discussed above, the Examiner's reasoning for combining Yim with O'Leary is inconsistent with the teachings of the Yim reference. As explained in the after-final office action response, Yim describes the use of calcium sulfate to reduce the preparation time or "set up time" of a composition comprising osteogenic proteins, autogenous blood and a porous particulate polymer matrix material. (column 2, lines 51-65). Presumably, calcium sulfate is useful in this composition to reduce setup time because of the relatively long period of time it takes for autogenous blood to clot in the formulation. Appellants note that this teaching is directly contrary to the present invention since the stated goal in Yim is to reduce set up time, not increase it.

Appellants' arguments are not persuasive because they are using the term "set up time" inconsistently. Yim uses the term "set up time" to be synonymous with "preparation time" of the composition. This is taken to mean the time to mix all of the ingredients to form a composition that is ready to be applied to the bone defect. In the art of hydration of calcium sulfate hemihydrate, "set time" is the time that any given calcium sulfate hemihydrate composition to harden. See previously cited GB 999,487, col. 1. Since the time a composition takes to harden is directly dependent upon the

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amount of calcium sulfate hemihydrate, the amount of hydrating solution and the presence and amount of any set retardant in the composition, the "set" time is fixed for any given combination of a known amount of calcium sulfate hemihydrate, a known amount of mixing solution and a known amount of set retardant. Therefore, the "set time" of the composition of Yim occurs after the composition has been prepared and administered (defined by Yim as the preparation time or "set up time"). These two times are only related insofar as it is clear that the composition must be administered after the "set up time" (i.e. after the composition is prepared) but cannot be administered after the "set time" (because the composition would be hardened at that time and could not be manipulated sufficiently to be placed into the desired defect).

Appellants state "Yim does not provide a general suggestion that calcium sulfate provides such advantages in all bone graft compositions." Appellants again assert that the teaching of the Yim reference must be limited to a suggestion to combine a calcium sulfate hemihydrate-containing substance (CSHS) with the formulation of U.S. Patent 5,171,579 that is a formulation of osteogenic proteins, a blood clot and a porous particulate polymer matrix. Appellants state

The Examiner responded to this argument in the Advisory Action by noting that Yim describes the addition of calcium sulfate hemihydrate to other compositions as well, such as the suggestion at column 2, lines 27-31 to form a composition containing calcium sulfate hemihydrate and an osteogenic protein. Yet, the Examiner continues to rely on the improved handling/moldability teaching in Yim as the motivating factor for the alleged combination. The Yim reference does not teach that improved handling/ moldability will be realized in the other embodiment noted by the Examiner. The osteogenic protein/calcium sulfate hemihydrate embodiment is described more fully at column 8, lines 16-28, where the reference teaches that, in that embodiment, calcium sulfate hemihydrate provides a structural matrix function, an osteoconductive matrix and a protein sequestering function. There is no discussion of improved handling whatsoever.

Appellants' arguments are misplaced. Again, there is no requirement that there be any express statement of benefit for every formulation disclosed by Yim. Further, it remains unclear as to why Appellants believe that all formulations of Yim (which are taught to contain calcium sulfate hemihydrate) would not all have the benefit that Yim specifically relates to the addition of the calcium sulfate hemihydrate. A composition and its properties are not separable. Appellants have provided no objective evidence of record to support this conclusion.

Appellants assert that there is no motivation to combine the teachings of Gertzman with O'Leary. Appellants focus on the differences between O'Leary and Gertzman but fail to address the similarities or the basis of motivation for combination set forth in the previous office actions. Appellants fail to address the fact that the first acknowledgement of the conventional use of allograft bone in bone growth promoting compositions is found in the Background of the Invention section of the patent at col. 1. This section is not discussing the invention of Gertzman and therefore provides a motivation to add a conventional ingredient to a bone growth promoting composition regardless of the invention claimed by Gertzman. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998). "The use of patents as references is not limited to what the patentees describe as their own inventions or to the problems with which they are

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concerned. They are part of the literature of the art, relevant for all they contain." In re Heck, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting In re Lemelson, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968)). However, the disclosure of the patent to Gertzman is germane since it shows that malleable pastes are preferred in treating bone defects and that numerous substances are well known to be included in compositions for treating bone defects such as autologous bone, allograft bone, bone marrow and blood.

Appellants continue to argue that Gertzman teaches away from the composition of O'Leary by pointing out the discussions in Gertzman which discuss a composition identified in Gertzman as GRAFTON® and is which is described as a "simple mixture of glycerol and lyophilized, demineralized bone powder of a particle size in the range of 0.1 cm to 1.2 cm." GRAFTON® is one of the embodiments of the invention disclosed by O'Leary. Appellants assert that the teaching of Gertzman, which notes that GRAFTON® has been "runny" when placed in vivo, as well as discussions in Gertzman about the potential toxicity of glycerol, is sufficient to teach away from the disclosure of O'Leary et al. However, review of col. 2, lines 40-55, shows that Gertzman states that GRAFTON®

"works well to allow the surgeon to place the allograft bone material at the site. However, the carrier, glycerol has a very low molecular weight (92 Daltons) and is very soluble in water, the primary component of the blood which flows at the surgical site.' Glycerol also experiences a marked reduction in viscosity when its temperature rises from room temperature (typically 22°C in an operating room) to the temperature of the patient's tissue, typically 37°C. This combination of high water solubility and reduced viscosity causes the allograft bone material to be "runny" and to flow away from the site almost immediately after placement', this prevents the proper retention of the bone within the site as carefully placed by the surgeon."

This "teaching away" appears to be limited to the use of glycerol component of GRAFTON®, specifically since the quote above constantly refers to glycerol and not the other ingredients. Since the teaching of O'Leary is not limited to the GRAFTON® composition (which is only one embodiment of the disclosed invention) and since disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments, Appellants' arguments are not persuasive. See *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). See also *In re Gurley*, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) ("A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use."). Further, it is noted that Appellants' claims recite "open" transitional phrasing and allow for the inclusion of multiple undisclosed and unclaimed ingredients, even in major amounts. Therefore, it is unclear why any discussion of the presence or absence of glycerol in the claimed invention is germane to the claims and rejection of record.

For the above reasons, it is believed that the rejections should be sustained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

This examiner's answer contains a new ground of rejection set forth in section (9) above. Accordingly, appellant must within **TWO MONTHS** from the date of this answer exercise one of the following two options to avoid *sua sponte* **dismissal of the appeal** as to the claims subject to the new ground of rejection:

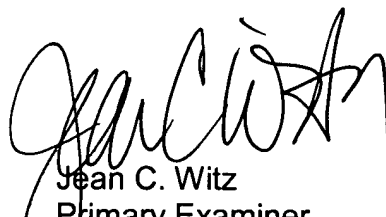
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(1) **Reopen prosecution.** Request that prosecution be reopened before the primary examiner by filing a reply under 37 CFR 1.111 with or without amendment, affidavit or other evidence. Any amendment, affidavit or other evidence must be relevant to the new grounds of rejection. A request that complies with 37 CFR 41.39(b)(1) will be entered and considered. Any request that prosecution be reopened will be treated as a request to withdraw the appeal.

(2) **Maintain appeal.** Request that the appeal be maintained by filing a reply brief as set forth in 37 CFR 41.41. Such a reply brief must address each new ground of rejection as set forth in 37 CFR 41.37(c)(1)(vii) and should be in compliance with the other requirements of 37 CFR 41.37(c). If a reply brief filed pursuant to 37 CFR 41.39(b)(2) is accompanied by any amendment, affidavit or other evidence, it shall be treated as a request that prosecution be reopened before the primary examiner under 37 CFR 41.39(b)(1).

Extensions of time under 37 CFR 1.136(a) are not applicable to the TWO MONTH time period set forth above. See 37 CFR 1.136(b) for extensions of time to reply for patent applications and 37 CFR 1.550(c) for extensions of time to reply for ex parte reexamination proceedings.

Respectfully submitted,



Jean C. Witz
Primary Examiner
Art Unit 1651


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A Technology Center Director or designee must personally approve the new ground(s) of rejection set forth in section (9) above by signing below:

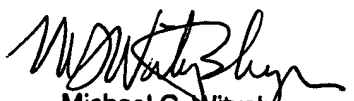
TC1600 Director:


Conferees:

Christina Chan


CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Michael Wityshyn


Michael G. Wityshyn
Supervisory Patent Examiner
Technology Center 1600


BRUCE M. KISLIUK
DIRECTOR
TECHNOLOGY CENTER 1600